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15th July 1986

Dear Mr. Holtzman,

Product Liability Liaison Group

In Michael Garner's absence, I attended the meeting of the Product Liability Liaison Group of the Tobacco Advisory Council on Monday 7th July.

There was, in fact, no meeting of the Group as such, since the Chairman suggested that it would be useful to attend a presentation given by Mr. Peter Lee, an independent consultant employed by the Tobacco Advisory Council from time to time to undertake studies on their behalf. The presentation, which was attended by about thirty people, dealt with the passive smoking issue. It may be that you have already received details of the work of Mr. Lee, but in case you have not, I outline his presentation below.

1. The "Passive Smoking" Studies

Mr. Lee had examined the results of 13 previous studies which had revealed that there was a statistical difference between the risk of a non-smoker who is married to a smoker contracting lung cancer and the lesser risk of a non-smoker

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15th July 1986

Two

married to another non-smoker contracting lung cancer. The persons who had compiled these studies had attributed this statistical difference to the "passive smoking" of the non-smoking partner who was married to a smoker.

The results of these studies varied considerably. Some showed that the risk of a non-smoker who was married to a smoker contracting lung cancer (by passive smoking) was doubled, whilst at the other end of the scale, some studies showed a slight reduction in that risk (no explanation was offered for such results by Mr. Lee). Mr. Lee said that the average risk of a non-smoker married to a smoker contracting lung cancer was revealed by the results of all such studies as being 1.3 (the risk of a non-smoker married to a non-smoker, and who does not therefore passively smoke, contracting lung cancer being 1.0).

2. The Bias in the "Passive Smoking" Studies

Mr. Lee's theory seems to be that the statistical difference in the risk of a non-smoker who is married to a smoker contracting lung cancer and a non-smoker who is married to a smoker contracting lung cancer is wholly or partly due to a bias caused by:-

(a) Some "passive" smokers being actual smokers who deny smoking; and

(b) The statistical effect of a smoker being accidentally mis-classified as a non-smoker (and vice versa) in the compilation and/or processing of the data used to obtain the results of the tests.

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15th July 1986

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3. The Salivary Cotinine Study

(a) The study undertaken by Mr. Lee sought to eliminate that part of the bias mentioned in 2(a) above, by using an objective test to determine whether some people who assert that they are non-smokers do in fact smoke. Mr. Lee took saliva samples from participants in his study and analysed them to reveal the existence of cotinine, a chemical produced by the inter-action of nicotine and saliva. In Mr. Lee's opinion, the samples revealed that 5.5% of men and 3.8% of women gave "discrepant" answers to the question whether they were smokers.

A histogram of the results of 984 salivary cotinine tests was circulated (although Mr. Lee said he had taken 1537 samples), a copy of which is enclosed. It seems to show that some of those purporting to be non-smokers, registered cotinine levels as high as the levels recorded by most of the smokers, and these people may be those who Mr. Lee thought had given "discrepant" answers although Mr. Lee did not state how he had arrived at the figures he had given for the "discrepant" answers.

It was not made clear how the study distinguished between a genuine non-smoker who might be affected by "passive smoking" so as to register a high cotinine level and a smoker who had given a "discrepant" answer. It may be that it is medically impossible for a non-smoker to register such levels of cotinine.

Mr. Lee said that the histogram shows that about 25% of the non-smokers did not have any cotinine in their saliva. Apparently, the trend is for the amount of

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15th July 1986

Four

cotinine in saliva to increase with the number of manufactured cigarettes smoked.

(b) Mr. Lee estimated that the statistical bias due to mis-classification mentioned in 2(b) above led to the results of all previous studies being 5% incorrect. If the results of the studies are adjusted to take this error into account, the risk of smokers contracting lung cancer seems to be reduced from 20 to 19.5 and the risk of non-smokers married to non-smokers contracting lung cancer is apparently increased from 1.0 to 1.5. In Mr. Lee's opinion, it is this mis-classification which accounts for the statistical difference in the results of the previous studies although the persons compiling such studies have attributed that difference to passive smoking.

The question of how to eliminate the 5% mis-classification was not mentioned and Mr. Lee did not say how he had dealt with this in his study.

4. Further Questions

There then followed a session during which Mr. Lee answered questions. Some of the technical aspects of the study were discussed (such as the metabolism of cotinine) and comments were made regarding the previous studies which Mr. Lee had mentioned. In particular, a Japanese study was compared with Mr. Lee's salivary cotinine study and the point was made that Japanese women may be particularly reluctant to admit that they are smokers thereby artificially increasing the apparent effects of passive smoking.

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15th July 1986

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Mr. Lee said that without further salivary cotinine studies in different countries, it was impossible to estimate the degree of distortion caused by any possible mis-representations of this type to the results of studies carried out in other countries.

5. Conclusions

Mr. Lee concluded that although a very small effect of passive smoking of about 1.5% could not be ruled out, the inherent bias in previous studies was about 1.2 (it was not clear how the figures of 1.5% and 1.2 were arrived at). If the results of these studies were adjusted to take this bias into account, it seems that the average risk of passive smoking (as revealed by the 13 previous studies) would be reduced from 1.3 to 0.1.

It was agreed that Mr. Lee's study was of significant importance in demonstrating the inherent bias in studies on the effects of passive smoking and in providing a more accurate, objective analysis of the true effects of passive smoking. However, it appears to us that it was not completely clear that Mr. Lee's study conclusively proved the point he wished to make.

Yours sincerely,



Zoe Tallis

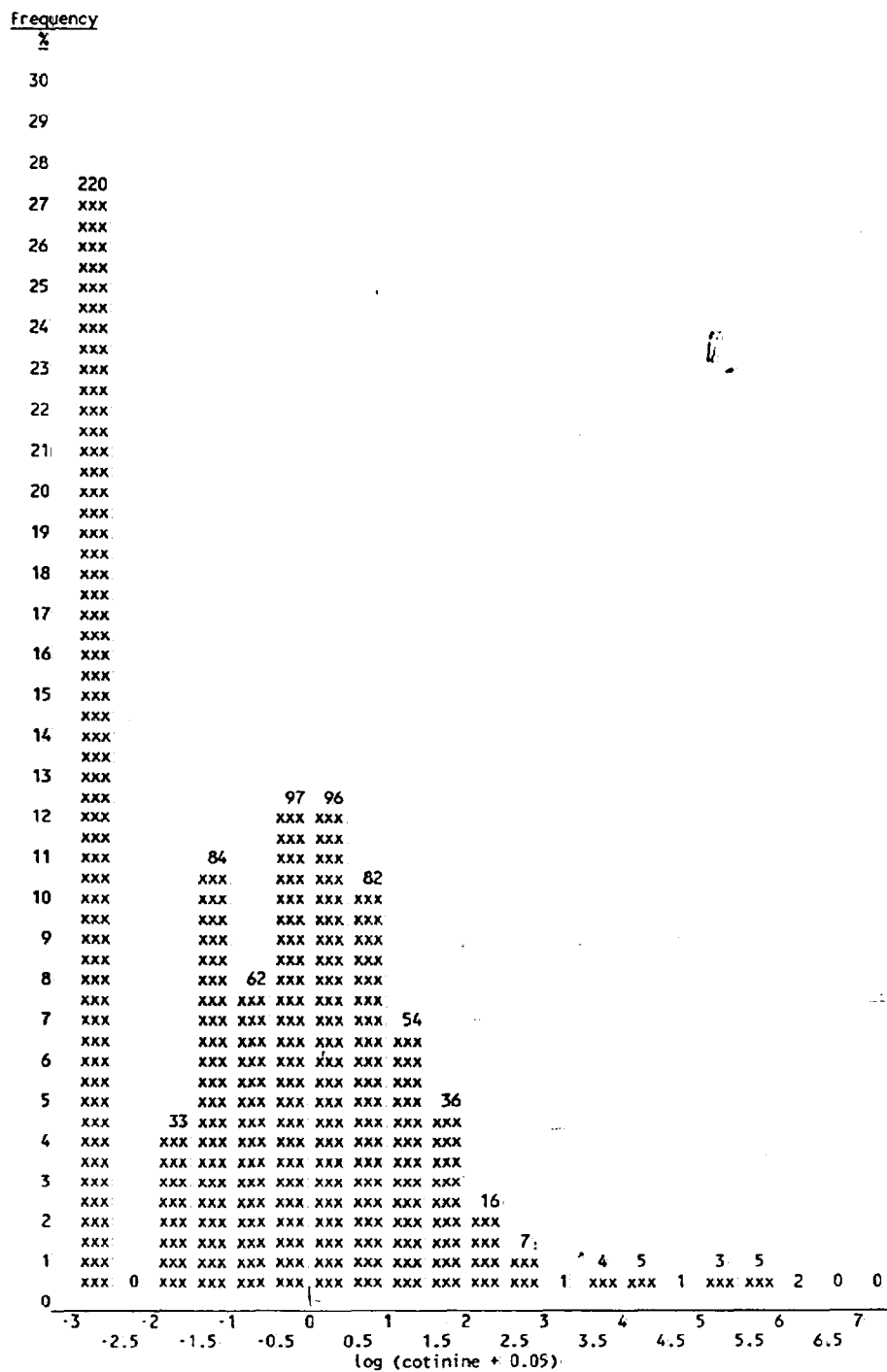
c.c. D. Hoel, Esq., Shook Hardy & Bacon.
E. D. Oxberry, Esq., Philip Morris, Feltham.
B. B. Brooks, Esq., Philip Morris, Lausanne.

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TABLE 10

Histogram of log (cotinine + 0.05) values for non-smokers
or users of other nicotine containing products



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